

FUNGI POSING OCCUPATIONAL HAZARDS IN AGRICULTURAL ENVIRONMENTS

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Fungi have long been known to affect humans and animals through actual infection of tissues, contamination of foodstuffs which contain toxic products produced by fungi, or by inducing allergic reactions.

Fungi have been considered primarily as pathogens of plants, however, some plant associated fungi are increasingly becoming agents of human disease.

OPPORTUNISTIC MYCOSES: These are fungal infections that occur mostly in patients with impaired defense mechanisms, but also can occur in otherwise healthy individuals or victims of severe trauma. Three major categories of fungi cause opportunistic mycoses.

1. The first group represents the fungi which are well-known as causes of the classical systemic mycoses and includes *Cryptococcus neoformans* (Sanfelice) Vuillemin (cryptococcosis), *Histoplasma capsulatum* Darling (histoplasmosis), and *Coccidioides immitis* Rixford et Gilchrist (coccidioidomycosis). These mycoses can occur in otherwise healthy individuals, however, they have assumed a new and important role as opportunistic infections. Cryptococcosis has for a number of years been a major threat to transplant patients, and all three are now important causes of opportunistic infection in AIDS (Acquired Immune Deficiency Syndrome) patients. The main defect in host defenses which predisposes to infection by these fungi is impaired cell-mediated immunity. This occurs as a result of immunosuppression in transplant patients, but is part of the normal disease process in AIDS [destruction of T-helper lymphocytes by human immunodeficiency virus (HIV)]. These fungi are acquired from the environment by inhalation of the blastospores (*Cryptococcus*), conidiospores (*Histoplasma*), or arthrospores (*Coccidioides*).

2. The second category is represented by yeast-like fungi, especially of the genus *Candida*. Infections by *Candida* and other yeast-like fungi are a serious threat to cancer and transplant patients and many other groups of patients with serious chronic illnesses. The defect in host defenses predisposing to *Candida* infection is frequently a combination of factors, including leukopenia (a condition in which the number of leucocytes circulating in the blood is abnormally low) which can be caused by chemotherapy, damage to mucosal lining by chemotherapy, disturbance of the normal microbial flora by antibiotic therapy, and disruption of the integrity of the normal skin and mucosal barrier by surgery or indwelling devices (catheters) allowing invasion by fungi. *Candida* is part of the normal flora of humans; thus, the infections are endogenous.

3. The third group of opportunistic fungal infections is caused by filamentous fungi. Of greatest importance are *Aspergillus fumigatus* Fresen. (Figs. 1 & 2), *A. flavus* Link:Fr. (Fig. 3), and the Zygomycetes *Rhizopus* spp. (Fig. 4) and *Mucor* spp. In recent years *Fusarium* spp. have also emerged as important human pathogens. These fungi are not part of the indigenous human flora and the infection is in most cases acquired by inhalation of spores. These fungi very rarely cause significant infection in healthy individuals, since inhaled spores are destroyed in the lungs by phagocytes. However, in severely leukopenic patients or patients with impaired phagocytosis due to high-dose steroid therapy, the spores germinate and invade the lung tissue. A characteristic of these fungi is to have an affinity for blood vessels. They destroy the blood vessel walls which may cause massive hemorrhage into the surrounding tissue. In addition, they cause clot formation ("thrombosis") within the blood vessels which leads to infarction (necrosis) of the tissue supplied by the blood vessel. This predilection for the blood vessels with destruction and occlusion explains the often fulminant (sudden and intense) course of these infections. A fatal infection limited to the lungs is most common, but spread to many other organs is not rare. Invasive infections by these molds are most common in transplant patients and cancer patients. For unknown reasons, Zygomycetes also cause serious infections in diabetic patients in ketoacidosis, i.e. poorly controlled diabetes. Here, the infection usually starts in the mouth or a paranasal sinus, but rapidly spreads to the eye and the brain.

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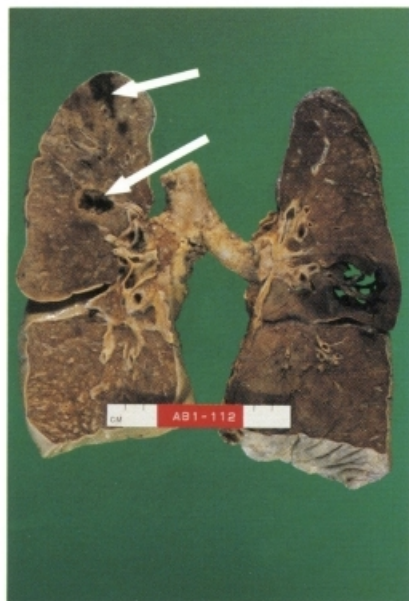


Figure 1. Lungs from kidney transplant patient with *Aspergillus fumigatus* infection. Necrotic and hemorrhagic lesions are indicated by arrows. (Formalin-preserved specimen.)

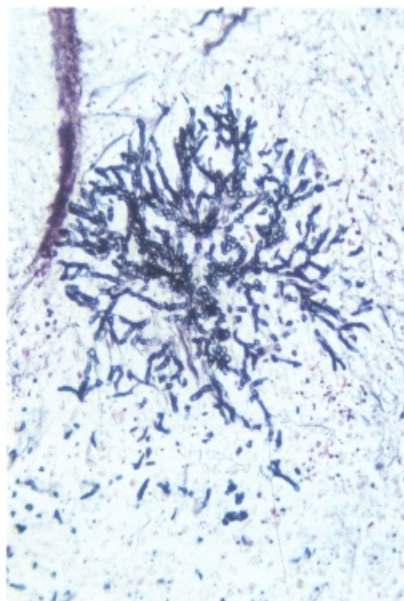


Figure 2. Microscopic section of *Aspergillus fumigatus* infection of lungs. Colony of hyphae growing in blood



Figure 3. Brain from liver and kidney transplant patient with *Aspergillus flavus* infection. Note large abscess (arrow) and blood (dark material) in



Figure 4. Necrotic and hemorrhagic lung lesion from a kidney transplant patient with *Rhizopus* infection. (Fresh specimen.)

ASPERGILLUS AND PENICILLIUM

Species of *Aspergillus* and *Penicillium* affect a wide variety of crops in the field and in storage. In the field, they affect grain crops, invade seed embryos, and cause seedling blights on germination (22, pp. 54, 56-57). *Aspergillus niger* Tiegh. causes crown rot of peanut (19, p. 33) and also causes black rot of citrus (23, p. 59). The rot may be predominantly internal with masses of black powdery spores being apparent only when the fruit is cut. Conidia disseminated in air currents

cause infection via injuries. *Penicillium aurantiogriseum* Dierckx (= *P. martensii* Biourge) causes crown rot of asparagus, a seedling disease, following freezing injury (11, p. 331). Post-harvest or storage rots are principally caused by species of *Aspergillus* and *Penicillium*. They occur alone or in combination with other fungi (22, pp. 56-57). *Penicillium digitatum* (Pers.:Fr.) Sacc. (green mold) and *P. italicum* Wehmer (blue contact mold) cause citrus fruit rot (11, p. 331). *Penicillium expansum* Link (blue mold) causes soft rot of many fruits such as apple, pear, avocado, pomegranate (11, p. 331). *Aspergillus* spp. cause rots of many fruits and some vegetables in storage (11, p. 306). *Aspergillus niger* is implicated in storage decay of strawberry fruits (15, pp. 71-72). Species of *Aspergillus* and *Penicillium* may colonize and infect grain in storage causing a reduction in feed and market value (22, p. 56). Internal infections decrease germinability. When infections are well established, embryos are killed (24, p. 11). Peanut seed is often attacked by species of *Aspergillus* and *Penicillium* (19, p. 37).

Species of *Aspergillus* and *Penicillium* are constantly present in the human environment. They are some of the most common airborne fungi and are widely distributed in soils throughout the world. Their presence leads to deterioration and spoilage of foodstuffs, whilst exposure to their spores frequently results in allergic reactions, often of a serious nature.

Some *Aspergillus* spp. produce toxic substances called mycotoxins, the most important of which is aflatoxin (3, p. 291). Aflatoxin was discovered in 1960 when more than 100,000 young turkeys and some 20,000 ducklings, pheasant and partridge poults died in England after having consumed Brazilian peanut meal that was discovered to be moldy. The fungus producing the potent toxin was *A. flavus* and the toxin was named aflatoxin (3, p. 291, and 22, p. 57). This name is now generally applied to a number of related toxins (3, p. 291). Aflatoxin B₁, present in corn (*Zea mays* L.), is among the most potent of known carcinogens. Ten to 20 parts per billion (ppb) of aflatoxin consumed regularly by sensitive young animals can result in liver cancer. Effects of aflatoxin as a toxin or carcinogen have been demonstrated in a wide variety of domestic animals and in human patients who inadvertently consumed contaminated peanut meal. Aflatoxin has been implicated in primary liver cancer in humans. An outbreak of hepatitis in India has been linked to moldy corn containing aflatoxin (22, p. 57). In 1977, 60% or more of the corn grown in the southeastern USA contained at least 20 ppb (µg/kg) of aflatoxin B₁ - the legal maximum permitted by the US Food and Drug Administration (FDA) for corn in interstate commerce (22, p. 57).

Asthmatic allergy to conidia of the various *Aspergillus* spp. is a well-known and defined disease (20, p. 568). About eight species of *Aspergillus* have consistently and authentically been involved in human infectious disease. *Aspergillus fumigatus* accounts for almost all diseases, both allergic and invasive. Allergic aspergillosis has also been caused by *A. flavus*, *A. ochraceus* K. Wilh., *A. nidulellus* R. A. Samson & W. Gams, *A. niger*, *A. terreus* Thom in Thom & Church, and *A. clavatus* Desmaz. Aspergillosis of the lungs may be caused by *A. fumigatus*, *A. terreus*, *A. flavus*, *A. nidulellus*, and *A. niveus* Blochwitz (20, p. 567). A manifestation of allergy to *Aspergillus* usually occurs in individuals who have repeated exposure to organic dust that is heavily laden with conidia and mycelial debris. One well-known example of this is "malt worker's lung", which occurs in brewery workers and is associated with moldy (usually *A. clavatus*) barley (21, p. 622). "Farmer's lung", an acute or chronic, sometimes fatal disease of persons continually exposed to moldy hay or similar material is a manifestation of sensitization to several allergens, principally spores of actinomycetes. Several fungi also cause the identical syndrome; *Aspergillus niger*, *A. fumigatus*, and *A. flavus*, and *Penicillium* spp. are frequently involved. "Farmer's lung" has now been found to be a frequent and serious occupational disease of worldwide distribution. It is more frequent in areas of high rainfall where conditions for mold growth on hay are optimum (20, p. 715).

Office workers have suffered the same disease owing to the growth of microorganisms in air conditioning vents (20, p. 715). Profuse growth of *A. fumigatus* in dust was found in a ventilating system which served as a source of heavy inoculum resulting in cases of endocarditis (inflammation of the lining of the heart and its valves) following heart surgery (20, pp. 566-567). Air inlets were also the source of heavy growth of *A. fumigatus* resulting in cases of aspergillosis in kidney transplant patients (20, p. 567). In cases of *Aspergillus* pneumonia, the ventilating system was a probable factor (20, p. 567).

Documented infection by members of the genus *Penicillium* is very rare. Bronchopulmonary penicilliosis has been the most frequently reported form of the disease (20, pp. 659-660).

The large number of species which constitute the genus *Aspergillus* occupy a wide spectrum of habitats in our environment. As a consequence, many have become economically important in either harmful or useful roles. Their beneficial role relates mainly to industrial processes, in particular the production of acids, vitamins and antibiotics. In the Orient certain species form the basic ingredient of traditional foods (14).

CLAVICEPS PURPUREA

Claviceps purpurea (Fr.:Fr.) Tul., the cause of ergot of rye, infects the young ovaries of the rye flowers by direct penetration and produces sclerotia that replace the seeds. The sclerotia of this fungus contain a number of poisonous alkaloids and are responsible for poisoning animals including humans. Cattle are often poisoned by grazing on cereals and grasses that carry the sclerotia of the various *Claviceps* spp. Their legs, hoofs and tails become gangrenous and cows may abort their calves. In the past, because of improper methods of cleaning the grain before grinding it into flour, human beings suffered from a horrible disease, which because of its symptoms, became known as "St. Anthony's Fire". Early symptoms included cold or prickling sensations in the limbs, followed by severe muscular pains. Affected limbs became swollen and inflamed with violent burning pains and sensations of intense heat. Mummification or moist gangrene ensued, and the extent of necrosis varied from the shedding of parts of fingers or toes to the loss of all four limbs. Many died, particularly in countries where the consumption of rye bread was high. The sclerotia of *C. purpurea* contain a number of powerful alkaloids such as ergotamine, ergometrin, and ergonovine, which are used medicinally to induce labor and prevent post partum hemorrhage during childbirth. These drugs are so useful that rye and wheat fields are artificially inoculated in Europe and elsewhere to increase sclerotial production, which in Portugal is a valuable source of income (3, pp. 340-342, 16).

FUSARIUM

Fusarium oxysporum Schlechtend.:Fr., an aggressive wilt pathogen of many plants (4), has infected and destroyed the lungs of dozens of immunocompromised patients and has in the last few years been identified for the first time in clinical infections (17). *Fusarium moniliforme* J. Sheld. causes ripe rot of figs, root, stalk, and pink kernel of corn (11, p. 317) and leaf spot diseases of ornamentals (5, p. 27). *Fusarium moniliforme* is a major parasite of several Gramineae such as rice, sugarcane, sorghum and others. On rice, it causes seedling blight, foot rot, stunting and hypertrophy of shoots (bakanae disease) (4, p. 125). When growing on corn or other grain, it produces a potent toxin. This toxin causes a disease called leukoencephalomalacia (LEM) in horses that consume the infected grain. The chemical nature of the mycotoxin that causes equine LEM is unknown (16). The affected animals show increasing ataxia (inability to coordinate voluntary muscular movements), and at autopsy large areas of necrosis in the brain are seen (20, pp. 712-713, 16). Other *Fusarium* species produce a variety of toxins when growing on fodder, forage, or grain. Vomitoxin is produced by the growth of *F. graminearum* Schwabe [*Gibberella zeae* (Schwein.) Petch] on corn. In small concentrations it induces vomiting in domestic animals; at concentrations of 1.4 ppm or more, however, feed is rejected by animals because of the bad taste (20, p. 713). In 1986, various *Fusarium* species were isolated from naturally contaminated ears of corn in southern Minnesota. When these isolates were single-spored, grown on sterile rice substrate, and fed to rats, *F. proliferatum* (T. Matsushima) Nirenberg caused hemorrhage, diarrhea, and death. This was the first report of *F. proliferatum* causing organ hemorrhage as well as death. *Fusarium subglutinans* (Wollenweb. & Reinking) P. E. Nelson, T. A. Toussoun, & Marasas caused death; *F. graminearum* caused uterine enlargement, hemorrhage, and death; *F. moniliforme* caused hemorrhage in various organs, diarrhea and death; and *F. oxysporum* caused hemorrhage and death. All isolates caused rats to gain less weight than those fed control diets (1).

Fusarium fungi produce metabolites belonging to a number of chemical groups (e.g., trichothecenes, zearalenone, moniliformin, and butenolide) under favorable environmental conditions (12, p. 9). The Sporotrichiella section contains the following most toxic species of fusaria: *Fusarium poae* (Peck) Wollenweb., *F. sporotrichoides* Sherb., *F. tricinctum* (Corda) Sacc., and *F. chlamydosporum* Wollenweb. & Reinking. These fungi produce toxic trichothecenes which have been associated with several outbreaks of intoxication in humans and animals through consumption of contaminated agricultural products (12, p. 10).

MYCOCENTROSPORA

Emmons et al. (9) reported a case of extensive verrucous lesions on the face of a 12-year-old Indonesian boy, from which they isolated a fungus identified as *Cercospora apii* Fresen. This fungus caused leaf spots on lettuce, tomato, and potato seedlings, was recovered from the diseased plants and was indistinguishable from that isolated from the human patient. Chupp (6) rejected this identification. Deighton and Mulder (7), by courtesy of the American Type Culture Collection, obtained the original isolation under the name *C. apii*, and reidentified it as *Mycocentrospora*, morphologically indistinguishable from *M. acerina* (R. Hartig) Deighton, a known plant pathogen having a wide host range.

RHIZOPUS

Infections are usually acquired by inhalation of sporangiospores. *Rhizopus oryzae* Went & Prinsen Geerligs is the species most frequently recovered in mucormycosis. *R. oryzae* (optimum 35°C) will grow at temperatures up to 45°C. Because *R. stolonifer* (Ehrenb.:Fr.) Vuill. (optimum 25°C) is inhibited by temperatures of 36°C and above, it is unlikely to be

pathogenic in warm-blooded animals (9). Both species cause rot of apples, apricots, cherries, nectarines, peaches, pears, and plums (22).

SPOROTHRIX SCHENCKII

Sporotrichosis, an infection caused by the fungus *Sporothrix schenckii* Hektoen & Perkins, affects the exposed parts of the body, namely the hands, arms and legs. It involves all layers of the skin and the subcutaneous lymphatics. The fungus produces an indolent lesion that may remain localized or may spread centrally through the local lymphatics, establishing a chain of nodules. It may also disseminate to become a generalized infection involving bones, joints, lungs and the central nervous system. The disease occurs most frequently in individuals such as farmers, nursery workers, gardeners, horticulturists, forestry workers, tree planters or orchid growers (2,8,18) who are exposed to material contaminated with *S. schenckii* because of their occupation. Infection is usually acquired by traumatic implantation with injury to skin caused by the prick of a thorn, splinter or similar object that is contaminated with *S. schenckii*. The disease can also affect domestic animals (8,18).

In 1984, the causal agent was isolated from 2 of 12 national brands of potting soil with significant frequency (13). Although sporotrichosis is not new to the nursery business, this is the first time that *S. schenckii* had been isolated from commercial growing media, which means it is now a concern in container as well as bare root nurseries.

Occasionally, inhalation of airborne conidia due to contact with contaminated sphagnum moss causes lung infections (2).

CONTROL: Cutaneous sporotrichosis does not respond to treatment with antibiotics or with local applications of antifungal preparations. Only orally administered potassium iodide (KI) given daily in milk, as a saturated solution of KI, is effective. Treatment should be continued for at least 4 weeks. Control of extracutaneous infections requires treatment with amphotericin B administered intravenously or in combination with 5-fluorocytosine, surgery or both (8,18).

Opportunistic mycoses may not respond well to currently available antifungal agents [Amphotericin B, flucytosine, miconazole, griseofulvin and others (10)]. Invasive mold infections have a very grim prognosis and attempts at prevention are made by keeping susceptible patients in a controlled environment with laminar air flow (sterile air supply). In reference to allergic and mycotoxin problems, avoiding exposure is the key to control.

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